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Docket No.: 1259-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Bojidar M. Stankov	)	Group Art: 1616
	)	Examiner: Choi, Frank I.
	)	
Serial No.: 09/854,802	)	
	)	
Filed: May 14, 2001	)	

For: CONTROLLED RELEASE FORMULATIONS CONTAINING AN ACTIVE INGREDIENT, PREFERABLY MELATONIN AND THE METHOD OF PREPARATION

New York, NY 10036
September 7, 2005

MS Appeal
Commissioner for Patents
P.O. BOX 1450
Alexandria, VA 22313-1450

SUBSTITUTE APPEAL BRIEF

This is an appeal from the final rejection of claims 16-18 and 20-24. This is the second Appeal Brief that has been filed in this application and under the provisions of 35 U.S.C.§134(a) no additional appeal fee is due.

(i) Real party in interest. The real party in interest is Ambros Pharma S.r.l.

(ii) Related appeals and interferences. There are no related appeals or interferences.

(iii) Status of the claims. Claims 1-15 and 19 have been canceled. Claims 16-18 and 20-24 are in the application and all of these claims have been finally rejected.

(iv) Status of amendments. An Amendment was filed with the original Brief to delete the mark "--" at page 8. This Amendment has not been entered. A petition, directed to the

objection to claims 17, 18, 20, 21 22, and 24 has been granted.

(v) Summary of claimed subject matter. The independent claims are claims 16 and 22. Claim 16 points out a formulation for the controlled release of melatonin that comprises (a) a slow release nucleus and a fast release cortex coating on the nucleus (page 4, lines 8-12). The components of the slow release nucleus are melatonin, hydroxypropyl methylcellulose, a lubricant, a volume excipient and a glidant (page 6, line 30 to page 7, line 2 and Example 1); the fast release cortex coating comprises melatonin, hydroxypropyl methylcellulose, a lubricant, a glidant and a volume excipient (page 7, line 4 and Example 1). The slow release nucleus is described in claim 16 as releasing 95% of the melatonin in a 5 period and the fast release cortex releases 95% of the melatonin in 10 minutes under the stated conditions. Claim 22 points out a formulation for the controlled release of melatonin that comprises (a) a slow release nucleus and a fast release cortex coating on the nucleus (page 4, lines 8-12). The components of the slow release nucleus and the fast release cortex are as defined in claim 16. The slow release nucleus is described in claim 16 as releasing 95% of the melatonin in 5-7 hours in vivo and the fast release cortex releases 95% of the melatonin in 5-10 minutes in vivo (page 4,lines 1-7).

(vi) Grounds of rejection to be reviewed on appeal.

Are claims 16-18, 20-24 unpatentable under 35 U.S.C§112, first paragraph, as not being enabled other than for the formulation set forth in Example 1?

Are claims 16-18, 20-24 unpatentable over 35 U.S.C.§112, first paragraph, as failing to comply with the written description requirement?

Are claims 16-18 and 20-24 unpatentable over 35

U.S.C.§112, second paragraph as being incomplete for omitting essential elements?

(vii) Argument.

The Rejection for Lack of Enablement

Claims 16-18 and 20-24 have been finally rejected under 35 U.S.C.§112, first paragraph, as not being based on an enabling disclosure. The disclosure is directed to one of ordinary skill in the art which involves the making of controlled release formulations for oral administration. The text of the application at pages 7-8 provides a detailed recipe for making an embodiment of the invention and the specification at pages 5-7 also provides additional information that enables a skilled worker in the art to make and use the claimed invention. The rejection of record takes the view that the one working Example of the present application is insufficient to provide enablement and that undue experimentation would be required to make and use the invention commensurate in scope with the claims.

Claim 16

Claim 16 points out controlled release formulations of melatonin as noted at page 1, lines 26-29 of the specification. This claim recites specific ingredients and release rates that are described in the original specification at pages 4, lines 8-12; page 7, lines 1-12. The referenced sections enable the skilled artisan to make and use the claimed invention.

Claims 17 and 20

Claims 17 and 20 are dependent on claim 16 and are enabled as

set forth above and in addition recite particular amounts of melatonin that are disclosed at page 4, lines 15-16.

Claim 18

Claim 18 is dependent on claim 16 which is enabled as noted above and in addition recites the preferred components as set forth in Example 1.

Claim 20 is dependent on claim 16 and is enabled for the reasons set forth above and in addition the specified amounts of melatonin are disclosed at page 4, lines 13-15.

Claim 21

Claim 21 is dependent on claim 16 which is enabled for the reasons set forth above and the maximum plasma levels are enabled by the disclosure at page 6, lines 5-8.

Claim 22

Claim 22 is an independent claim which is enabled for the reasons set forth above for claim 16 and in view of the preferred in vivo release rates as disclosed at page 4, lines 1-7.

Claims 23 and 24

Claims 23 and 24 are dependent on claim 16 and point out the method of inducing and maintaining sleep in one suffering from a sleep disorder by the use of the formulation of claim 16. The method is enabled by the description at pages 3, line 24 to page 4, line 30.

The provisions of 35 U.S.C.§112, first paragraph require that the disclosure of a patent application must be enabling. The enabling standard does not require that a claim

point out each and every detail and component of a preferred embodiment. The requirement of the first paragraph of Section 112 is only properly challenged when it is "reasonable" to conclude that one skilled in the art would be unable to carry out the claimed invention. In re Buchner, 929 F.2d 660; 18 USPQ2d 1331 (Fed. Cir. 1991). The present invention is concerned with controlled release of a single distinct entity, i.e. melatonin and not a multiplicity of different active ingredients which could pose different formulation issues based on differences in solubility, density, particle size, pH, dosage size, metabolic rats, sites of absorption, stability etc. which typically cause problems in preparing controlled release formulations.
The Examiner has not acknowledged that only a single active agent is pointed out by the finally rejected claims.

The text of Example 1 illustrates in great detail a working embodiment of a controlled release formulation of melatonin with the particular elements of the claims, i.e. HPMC, a lubricant, a volume excipient and a glidant. This information coupled with the general directions to those who are skilled in the art on pages 5 and 6 of the specification and the knowledge of the skilled artisan make it apparent that only with a minimum amount of experimentation, is it possible to make useful compositions within the scope of the claims other than the preferred embodiment of Example 1.

Enablement is determined on whether or not the extent of the experimentation necessary to practice the invention is reasonable. In re Wands, 858 F.2d 731; 8 USPQ2d 1400 (Fed. Cir. 1988). The Examiner has not evaluated the seven Wands factors which are: (a) breadth of the claims; (b) nature of the invention; (c) state of the art; (d) level of skill in the art; (e) level of predictability; (f) amount of direction provided by the inventor; (g) existence of working examples; and (h) the quantity of experimentation need to make and use the invention. When each of the Wands factors is evaluated, it is submitted that the present specification is enabling. For these reasons, it is requested that the rejection for lack of

enablement be reversed.

The text of claim 16 recites the principal ingredients as disclosed in the specification for making an operable composition. These claims are specific to a particular material and from this perspective are quite narrow. The recitation of the other ingredients is made in terms that are specific of to materials or classes of materials that are well known and are exemplified in the specification. The art of making controlled release formulations for oral administration to humans has generated many thousands of patents in recent years and there are many textbooks and courses that have been devoted to this subject. Since the present claims deal with only one substance, this variable is not present in the appealed claims. According to the standards set forth in MPEP§2164.04, the Examiner has not sustained the burden of showing a reasonable basis exists on which to challenge the claims.

The Rejection for Lack of a Written Description

Claims 16-18 and 20-24 have been finally rejected under 35 U.S.C.§112, first paragraph, as failing to comply with the written description requirement.

In evaluating a patent application for compliance with the written description requirement, there is a strong presumption that the claimed invention is present in the specification. In re Wertheim, 541 F.2d 257; 191 USPQ 90 (CCPA 1976). MPEP§ 2163 IIA. In addition, the Examiner has the initial burden of showing there is a lack of compliance with the written description requirement. MPEP§2163.04.

The reasons advanced by the Examiner are based on the use of the term "releases the melatonin within 5 hours..and within 10 minutes" which the Examiner contends reads on release in less than the stated time period. The reported performance criteria has to do with release of a stated time within a certain elapsed time. It is not concerned with a release of less than the stated but only total release after a

stated time. For these reasons, this ground of rejection should be reversed.

The Rejection Under 35 U.S.C.§112, second Paragraph

Claims 16-18 and 20-24 have been finally rejected under 35 U.S.C.§112, second paragraph, as being incomplete in that the elements of (a) granulation; (b) addition of retard excipient; and (c) application of melatonin solution under pressure are essential for the preparation of the formulations. MPEP §2172.01 was cited as authority for this ground of rejection.

This ground of rejection is in error because the claims are directed to controlled release tablets and methods of inducing sleep and not to the process of making the claimed tablets which are used in the claimed methods. The disclosure of preferred methods of making the invention does not mean that the product claims that recite what the applicant regards as the invention, must recite the preferred methods or even critical processing steps in order to define the product of the invention. The product may be defined apart from the method by which it is made as a new composition of matter. For this reason, it is not necessary to import into the product claims the preferred process by which they are made. The applicant is not required to recite the processing details of the best mode for the practice in all claims merely because he has described the best mode in explicit language. MPEP§ 2172.01 does not require that essential processing procedures have to be recited in a product claim. Only essential elements have to be recited regarding the elements of the product. This has been done. Claims 17, 18, 20, 21, 22 and 24 have been specifically noted by the Examiner as not indicating the presence of a lubricant. These claims are all dependent on claim 16 which explicitly recites that a lubricant is present.

For these reasons, it is requested that the rejections of record be reversed and patent protection allowed to an advance in the art.

Respectfully submitted,

James V. Costigan
Reg. No. 25,669

MAILING ADDRESS:
HEDMAN & COSTIGAN, P.C.
1185 Avenue of the Americas
New York, NY 10036-2601
(212) 302-8989

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(viii) Appendix.

16. A controlled release melatonin tablet which comprises:
(a) a slow release nucleus comprising melatonin, hydroxypropyl methylcellulose, a lubricant, a volume excipient and a glidant, wherein 95% of the melatonin is released within 5 hours in an oscillating tray containing gastric/intestinal juice at 37°C;
(b) a fast release cortex coating on said nucleus which comprises melatonin, hydroxypropyl methylcellulose, a lubricant, a volume excipient and a glidant, wherein at least 95% of the melatonin is released within 10 minutes in an oscillating tray containing gastric/intestinal juice at 37°C.

17. The melatonin tablet as defined in claim 16 which comprises:
(a) a slow release nucleus comprising from 1 to 3 mg of melatonin, hydroxypropyl methylcellulose, a volume excipient and a glidant;
(b) a fast release cortex coating on said nucleus which comprises 0.5-1.5mg of melatonin, and hydroxypropyl methylcellulose, a volume excipient and a glidant.

18. The melatonin tablet as defined in claim 16 which consists essentially of:
(a) a slow release nucleus consisting essentially of melatonin, and hydroxypropyl methylcellulose, a volume excipient and a glidant;
(b) a fast release cortex coating on said nucleus which consist essentially of melatonin, and hydroxypropyl methylcellulose, a volume excipient and a glidant.

20. The melatonin tablet as defined in claim 16 which consists essentially of:
(a) a slow release nucleus consisting essentially of 1-3 mg of

melatonin, hydroxypropyl methylcellulose, a volume excipient and a glidant;
(b) a fast release cortex coating on said nucleus which consists essentially of 0.5-1.5 mg of melatonin with hydroxypropyl methylcellulose, a volume excipient and a glidant.

21. The melatonin tablet as defined in claim 16 which comprises:
(a) a slow release nucleus comprising melatonin, and hydroxypropyl methylcellulose, a volume excipient and a glidant;
(b) a fast release cortex coating on said nucleus comprising melatonin, hydroxypropyl methylcellulose, a volume excipient and a glidant wherein said tablet provides a maximum plasma level of 1,000 to 2,000 pg/ml of melatonin upon in vivo administration.

22. A controlled release melatonin tablet which comprises:
(a) a slow release nucleus comprising melatonin, hydroxypropyl methylcellulose, a volume excipient and a glidant which releases the melatonin over a 5 to 7 hour period in vivo;
(b) a fast release cortex coating on said nucleus comprising melatonin, hydroxypropyl methylcellulose, a volume excipient and a glidant which releases the melatonin in 5-10 minutes in vivo.

23. A method of inducing and maintaining sleep which comprises the administration of the formulation of claim 16 to one who suffers from a sleep disorder.

24. A method of inducing and maintaining sleep which comprises the administration of the formulation of claim 20 to one who suffers from a sleep disorder.